RESPONSE

SUMMARY OF THE INVENTION

The present claims are directed to novel murine cell lines comprising a genetically engineered mutation in the mouse ortholog of a human gene. Like most patented cell lines, the described cells are useful as tumor models, for the expression of genetically engineered products, and for the identification and characterization of biochemical pathways. *Unlike* most patented cell lines, certain embodiments of the described cells are totipotent embryonic stem cells. As totipotent cells, embryonic stem cells have a normal compliment of chromosomes (unlike most patented aneuploid cell lines) and can thus be introduced into an embryo (by microinjection , morula aggregation, etc.) and used to produce animals that are essentially wholly derived from the manipulated ES cell's genetic material. When, as in the present case, the ES cell clone has been manipulated *in vitro* to contain a genetically engineered allele, the ES cell clone can be used to generate live animals capable of germ line transmission of the genetically engineered allele. These animals can then be used to determine the physiological function of the mutated gene through standard genetic analysis (which discerns the normal function of a gene via which physiological systems are perturbed by the engineered alteration of gene function). This basic approach to discerning the physiological role of genes has been embraced by the broader scientific community (see, for example, Exhibit A). In the present instance, when a certain embodiment of the claimed mutated cells (*i.e.*, an ES line embodiment) was used to produce animals homozygous for the mutation in the murine locus that naturally encodes the exon sequence described in SEQ ID NO:2, the resulting animals produced as taught in the specification displayed marked hyperactivity. These data reveal that the gene mutated in the described ES cell line may present a novel target for drug intervention in the treatment of, *inter alia*, attention deficit hyperactivity disorder (*i.e.*, a drug that antagonizes the targeted protein, in this case the CACNG8 protein, should impact the same physiological pathway contributing to the observed hyperactivity since the described animals have been genetically manipulated to presage the action of a "perfect" drug– a drug that specifically targets and ablates the function of the targeted protein). Given the clear medical importance of behavioral disorders in western medicine (not to mention classrooms), it is clear that the above discovery clearly defines a patentable and useful invention.

In summary, a review of patents issued over the last several decades indicates that non-totipotent cell lines constitute patentable subject matter (5,985,290, 5,288,628, etc.), ES cell lines constitute patentable subject matter (U.S. Patent No. 6,200,806), vectors and methods of genetically manipulating